

09-068804

## PATENT COOPERATION TREATY

VBB

JKF

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To: JANIS K. FRASER  
FISH & RICHARDSON P.C.  
225 FRANKLIN ST.  
BOSTON, MA 02110-2804

RECEIVED

OCT 06 1997

FISH & RICHARDSON P.C.  
BOSTON, MADate of Mailing  
(day/month/year)

03 OCT 1997

Applicant's or agent's file reference  
00786/292WO1

REPLY DUE

within TWO months  
from the above date of mailing

International application No.

PCT/US96/18504

International filing date (day/month/year)

14 NOVEMBER 1996

Priority date (day/month/year)

14 NOVEMBER 1995

International Patent Classification (IPC) or both national classification and IPC  
Please See Supplemental Sheet.

Applicant

THE GENERAL HOSPITAL CORPORATION

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Docketed by Billing Secretary

Due Date: \_\_\_\_\_

Deadline: \_\_\_\_\_

Initials: \_\_\_\_\_

Docketed by Practice Systems

PCT 2m Written Opinion 12-3-97

PCT Lack of Unity 11-3-97

Initials: ACRecord: 12981612988

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 14 MARCH 1998Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

H. F. SIDBERRY

Telephone No. (703) 308-0196

## International application No.

## I. Basis of the opinion

☒ the international application as originally filed.

☒ the claims, Nos. 1-45, as originally filed.  
 Nos. NONE, as amended under Article 19.  
 Nos. NONE, filed with the demand.  
 Nos. NONE, filed with the letter of \_\_\_\_\_

2. The amendments have resulted in the cancellation of:

☒ the drawings, sheets/fig NONE

4. Additional observations, if necessary:

Form PCT/IPEA/408 (Box I) (January 1994)★

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 3, 5, 11-15, 20-45

because:

- ☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 3, 5, 11 are so unclear that no meaningful opinion could be formed (*specify*).

A sequence listing is required for all disclosures of sequence information in which the sequence has four or more amino acids or ten or more nucleotides. The PCT application does not comply with Section 1.821(e), (a printable copy of the "Sequence Listing") a computer readable form, as defined in Section 1.821(e), 1.822 and 1.823, recorded as a single file on either a diskette or a magnetic tape. The claims recite Sequence Identifiers, but do not comply with the stated requirements, and therefore, no meaningful opinion could be written for claims 3, 5 and 11.

- ☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. (See Attached).

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IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees the applicant has:

- ☒ restricted the claims. (See Supplemental Sheet)
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1 not to invite the applicant to restrict or pay additional fees:

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1, 4, 10, 16-19, species of SspC.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	NONE	YES
	Claims	1, 4, 10, 16-19	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1, 4, 10, 16-19	NO
Industrial Applicability (IA)	Claims	1, 4, 10, 16-19	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1, 4, 10 and 16-19 lack novelty under PCT Article 33(2) as being anticipated by THE GENERAL HOSPITAL CORPORATION (WO 95/02048).

WO 95/02048 disclose DNA which encodes a substantially pure Salmonella secreted protein (Ssp). Applicant has defined a Salmonella secreted protein to be one where the secretion of the protein is dependent on expression of PrgH.

Disclosed is the gene which encodes PrgH (see pages 5, 11, 19). Disclosed is administration of mutants which have the gene (increase the express of the gene) or do not have the gene to express PrgH (decrease the expression of the gene), to mice (see pages 99 and 109).

Claims 1, 4, 10 and 16-19 lack novelty under PCT Article 33(2) as being anticipated by Hueck et al.

Hueck et al (Molecular Microbiology, 1995) disclose substantially pure DNA encoding a salmonella secreted protein, where the DNA comprises the SspB, SspC, the SspD and SspA gene (see page 479, Summary; page 483, Figure 4; page 485, Figure 6). Further disclosed is a "cell" which contains the DNA, (Salmonella typhimurium). The wild-type bacteria inherently contains this gene.

Claims 1, 4 and 10 lack novelty under PCT Article 33(2) as being anticipated by Kaniga et al.

Kaniga et al (Journal of Bacteriology, 1995) disclose DNA which encodes a Salmonella secreted protein, the DNA comprises the sipB and sipC genes which are analogous to SspB and SspC genes of the claims (see page 3968, Figures 4 and 5).

Claims 1, 4 and 10 lack novelty under PCT Article 33(2) as being anticipated by Hermant et al.

Hermant et al (Molecular Microbiology, 1995) disclose DNA which encodes a Salmonella secreted protein, the DNA comprises the sipEBCDA gene which is analogous to SspABCD gene recited in the claim. (Continued on Supplemental Sheet.)

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**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

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**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**TIME LIMIT:**

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:  
IPC(6): C07H 19/00, 21/00, 21/04; C12N 1/21; C12Q 1/02, 1/10, 1/18, 1/24; G01N 33/569 and US Cl.: 536/22.1, 23.7; 435/7.2, 7.32, 7.35, 29, 30, 32, 38, 252.1

**III. NON-ESTABLISHMENT OF OPINION:**

No international search report has been established for claim numbers 3, 5, 11-15, 20-45.

**IV. LACK OF UNITY OF INVENTION:**

1. This response is made to a telephone Lack of Unity requirement (see telephone memorandum attached hereto or attached to a prior Written Opinion).

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

Claims 1, 4, 10 and 16-19 meet the criteria set out in PCT Article 33(4).

**NEW CITATIONS**

KANIGA et al. Homologs of the *Shigella* IpaB and IpaC Invasins are Required for *Salmonella typhimurium* cultured Epithelial Cells. Journal of Bacteriology. July 1995, Vol. 177, No. 14, pages 3965-3971, see page 3968.

HERMANT et al. Functional conservation of the *Salmonella* and *Shigella* effectors of entry into epithelial cells. Molecular Microbiology. August 1995, Vol. 17, No. 4, pages 781-789, see pages 781 and 784.

**CHAPTER II  
PCT TELEPHONE MEMORANDUM  
FOR  
LACK OF UNITY OF INVENTION**

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PCT No.: PCT/US96/18504  
Examiner: H. F. SIDBERRY  
Attorney spoken to: A. MEIKLEJOHN  
Date of call: 20 AUGUST 1997

- ☐ Amount of payment approved:
- ☐ Deposit account number to be charged:
- ☐ Attorney elected to pay for ALL additional inventions
- ☐ Attorney elected to pay only for the additional inventions covered by
  - ☐ Group(s):
  - encompassing --
  - ☐ Claim(s):
- ☒ Attorney elected **NOT** to pay for any additional inventions, therefore, only the main invention, Group I, species of SspC, covered by Claim(s) 1, 4, 10, 16-19 has been examined.
- ☒ Attorney was orally advised that there is no right to protest for any group not paid for.
- ☒ Attorney was orally advised that any protest must be filed no later than 1 Month from the mailing of the Opinion (Form PCT/IPEA/408) or the Final Report (Form PCT/IPEA/409).

**Time Limit For Filing A Protest**

Applicant is hereby given 1 Month from the mailing date of this Opinion/Final Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 68.3, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

**Detailed Reasons For Holding Lack of Unity If Invention:**  
*(Continued on a separate sheet)*

**Note: A copy of this form must be attached to the Opinion/Final Report.**

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**ATTACHMENT TO CHAPTER II PCT TELEPHONE MEMORANDUM  
FOR  
LACK OF UNITY OF INVENTION**

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**Itemized Summary Of Claim Groupings:**

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1, 2, 4, 10 and 16-19, drawn to DNA encoding a Salmonella secreted proteins (Ssp), cell, method of inducing the uptake of bacteria.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

species of DNA encoding the Salmonella secreted protein.

The claims are deemed to correspond to the species listed above in the following manner:

Claim 2, the SspB DNA

Claim 4, the SspC DNA

The following claim(s) are generic: Claims 1, 10, and 16-19.

**Detailed Reasons For Holding Lack Of Unity Of Invention:**

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: because each DNA encodes and each protein species is directed to an antigen which differs physicochemically, antigenically, structurally and functionally.